between the reference compound and the compound of example 72. However, in going from the compound of example 72 to the compound of example 9, where the only structural difference is the replacement of the phenyl in the compound of example 72 with the benzyl group in the compound of example 9, a more striking difference in the shift in antiviral activity with increase in human serum level is seen. The compound of example 9 shows a shift of only about 3.3 (1.7/0.52=3.3) in antiviral activity compared to the 33.4 fold shift for the compound of example 72., i.e., the antiviral activity of the compound of example 9 changes much less (about 11 fold less) than the compound of example 72 in the presence of increasing amount of human serum. Therefore, it can be reasonably concluded that this unexpected difference in the antiviral activity of the compound of example 9 is due to replacement of the phenyl group on the N atom in the compound of example 72 to the benzyl group in the compound of example 9. Furthermore, in view of the above, it can also be concluded that, in comparing the reference compound with the compound of example 9, it is the replacement of the nitrogen phenyl with the nitrogen benzyl, rather than the replacement of the dimethylbenzyl with dimethylpyrimidyl that is primarily responsible for the unexpected shift in antiviral activity. These clarifications have also been made in the attached Rule 132 declaration.

As set forth in the Declaration, based on the data set forth therein, the compound of Example 9 would be favored over the reference compound in that it has reduced plasma protein bind and reduced shift in antiviral activity in human plasma. The compound of example 9 should be expected to interact with the desired receptor (CCR5) with higher efficiency in-vivo. A number of references have been made of record in the present case by the Applicants that discuss the concept of plasma protein binding in drug discovery. These references (e.g., *Expert Opinion. Drug Discov. (2007) 2(1): 51-64*) make it clear that the presence of free or unbound drug can lead to an effective attenuation of drug potency *in vivo*.

The presently claimed compounds have been limited to only those compounds wherein R^1 is $\S\!\!-\!\!M\!\!-\!\!R^4$: wherein M is aryl, substituted with R^4, and wherein R^2 is arylalkyl. Applicants respectfully submit that the scope of the claims presented herein is reasonably commensurate with the data presented in the declaration. The Examiner is respectfully requested to withdraw the present rejection.

Remarks

Claims 1-20 and 31-40 were previously canceled. Claims 21-30 are pending in the present Application. In the present paper, Applicants have amended claims 21-26, and 29-30.

Applicants wish to thank the Examiner for the interview granted to the undersigned attorney and Dr. Michael Miller on October 18, 2007.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 21-22, 24-26, and 29-30 under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement. The Examiner has alleged that solvates of the compounds of the invention have not been enabled. Without acquiescing to the Examiner's allegation, Applicants have canceled the word "solvate" from the claims, thus obviating the present rejection.

Rejection under 35 U.S.C. §103

Pending claims 21-30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Albert '920 supplemented with the GB '876.4.

As set forth in the Office Action dated June 20, 2007, in considering Applicants' Declaration under 37 CFR 132, and further explained in the interview, the Examiner is of the opinion that that the comparison between the reference compound and the compound of example 9 is not a vis-à-vis comparison; that there are two differences in that the compound of example 9 has a benzyl group vs a phenyl group in the reference compound, and a dimethylpyrimidyl vs a dimethylphenyl in the reference compound. The Examiner has asked for further clarification showing how Applicants arrived at the conclusion that the compound of example 9 possesses unexpected advantages over the reference compound.

In response, Applicants would like to point out that in comparing the reference compound with the compound of example 72, only one structural difference is seen, viz., replacement of the dimethylphenyl with dimethylpyrimidyl. In Table 2 of the declaration, it is seen that the shift in antiviral activity with increase in human serum level is approximately of the same order of magnitude for both the reference compound (44/0.90=48.9 fold shift) and the compound of example 72 (32/0.95=33.4 fold shift), i.e., there is only about 1.5 fold (48.9/33.4= 1.5) change in magnitude

CONCLUSION

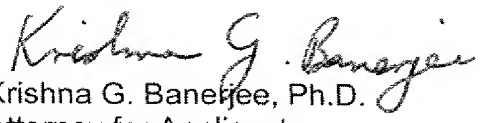
Applicants respectfully request prompt reconsideration of present claims 21-30, and an early allowance of the application.

If the Examiner wishes to comment or discuss any aspect of this application or response, applicants' undersigned attorney invites the Examiner to call him at the telephone number provided below.

December 20, 2007

Schering-Plough Corporation
2000 Galloping Hill Road
Patent Department, K-6-1, 1990
Kenilworth, NJ 07033
Tel: (908) 298-2135
Fax: (908) 298-5388

Respectfully submitted,



Krishna G. Banerjee, Ph.D.
Attorney for Applicants
Reg. No. 43,317